(FILE 'HOME' ENTERED AT 07:11:20 ON 15 FEB 2005)

FILE 'REGISTRY' ENTERED AT 07:11:29 ON 15 FEB 2005
L1 1 S DONEPEZIL/CN

FILE 'CAPLUS' ENTERED AT 07:11:53 ON 15 FEB 2005
L2 18 S L1/P

FILE 'REGISTRY' ENTERED AT 07:13:43 ON 15 FEB 2005
L3 1 S DONEPEZIL HYDROCHLORIDE/CN

FILE 'CAPLUS' ENTERED AT 07:14:11 ON 15 FEB 2005
L4 26 S L3/P
L5 4 S (L2 OR L4) AND ?CYCLIZ?

=> s (l2 or l4) and hydrogena?
265402 HYDROGENA?
L6 13 (L2 OR L4) AND HYDROGENA?

=> d bib hit 1-13

L6 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:29309 CAPLUS
DN 142:113913
TI Catalytic **hydrogenation** process for the preparation of intermediates for acetyl cholinesterase inhibitors
IN Reddy, Bandi Parthasaradhi; Reddy, Kura Rathnakar; Reddy, Rapolu Raji; Reddy, Dasari Muralidhara
PA Hetero Drugs Limited, India
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2005003092 | A1 | 20050113 | WO 2003-IN232 | 20030701 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI WO 2003-IN232 20030701
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Catalytic **hydrogenation** process for the preparation of intermediates for acetyl cholinesterase inhibitors
AB A simple industrial process for the preparation of the intermediates of acetyl cholinesterase inhibitors [I; R = H, lower alkoxy; Y = H, F; n = 1-4; e.g., 4-[(5,6-dimethoxy-1-indanon)-2-yl]methylpiperidine hydrochloride] is described which comprises the **hydrogenation** of the corresponding 4-pyridyl analog prepared by **hydrogenated** using a platinum oxide, Pt/C, raney nickel, or ruthenium oxide catalyst in the presence of an acid (e.g., aqueous HCl) under a pressure of 1-10 bars to give the 4-piperidinyl intermediate [II; e.g., 5,6-dimethoxy-2-(4-pyridyl)methyl-1-indanone].
ST dimethoxypyridylmethylindanone prepn catalytic **hydrogenation** dimethoxyindanonylmethylpiperidine

IT Amines, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(aromatic; catalytic **hydrogenation** process for the preparation of intermediates for acetyl cholinesterase inhibitors)

IT **Hydrogenation**
(catalytic **hydrogenation** process for the preparation of intermediates for acetyl cholinesterase inhibitors)

IT Acids, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(catalytic **hydrogenation** process for the preparation of intermediates for acetyl cholinesterase inhibitors)

IT Amines, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(cyclic; catalytic **hydrogenation** process for the preparation of intermediates for acetyl cholinesterase inhibitors)

IT Amines, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(salts; catalytic **hydrogenation** process for the preparation of intermediates for acetyl cholinesterase inhibitors)

IT 7440-44-0, Activated carbon, uses
RL: CAT (Catalyst use); USES (Uses)
(activated, support; catalytic **hydrogenation** process for the preparation of intermediates for acetyl cholinesterase inhibitors)

IT 7440-02-0, Raney nickel, uses
RL: CAT (Catalyst use); USES (Uses)
(catalysts; catalytic **hydrogenation** process for the preparation of intermediates for acetyl cholinesterase inhibitors)

IT 7440-05-3, Palladium, uses 11113-84-1, Ruthenium oxide 11129-89-8, Platinum oxide
RL: CAT (Catalyst use); USES (Uses)
(catalytic **hydrogenation** process for the preparation of intermediates for acetyl cholinesterase inhibitors)

IT 64-19-7, Acetic acid, reactions 1333-74-0, Hydrogen, reactions 4803-57-0 7647-01-0, Hydrogen chloride, reactions 7664-38-2, Phosphoric acid, reactions 7664-93-9, Sulfuric acid, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(catalytic **hydrogenation** process for the preparation of intermediates for acetyl cholinesterase inhibitors)

IT 120013-39-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(catalytic **hydrogenation** process for the preparation of intermediates for acetyl cholinesterase inhibitors)

IT 120014-30-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(catalytic **hydrogenation** process for the preparation of intermediates for acetyl cholinesterase inhibitors)

IT **120011-70-3P**, Donepezil hydrochloride
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L6 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:802718 CAPLUS
DN 141:314158
TI Process for the preparation of donepezil and derivatives thereof
IN Kumar, Yatendra; Prasad, Mohan; Nath, Asok; Maheshwari, Nitin
PA Ranbaxy Laboratories Limited, India
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004082685 | A1 | 20040930 | WO 2004-IB843 | 20040322 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI IN 2003-DE352 A 20030321

OS CASREACT 141:314158; MARPAT 141:314158

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB A process for the preparation of donepezil and its derivs. of formula I (R1-R4 = independently H, straight or branched -chain alkyl, alkoxy, alkoxycarbonyl, etc.; or a salt thereof), which comprises reducing 2-(4-pyridyl)methyl-1-indanone of formula II, is disclosed. For example, reaction of 5,6-dimethoxyindan-1-one with pyridine-4-carboxaldehyde, followed by **hydrogenation** and substitution with benzyl bromide, gave donepezil•HCl, which is 1-benzyl-4-[(5,6-dimethoxy-1-indanone)-2-yl]methylpiperidine. Thus, the present invention provides a process for the preparation of donepezil or a pharmaceutically acceptable salt thereof, and pharmaceutical compns. that include the donepezil or a pharmaceutically acceptable salt thereof, which are active compds. for the treatment of CNS disorders.

IT 81270-45-3P, 2-(4-Piperidinyl)methyl-1-indanone **120011-70-3P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of donepezil and derivs.)

L6 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:652671 CAPLUS

DN 141:174080

TI **Hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride)

IN Radhakrishnan, Tarur Venkatasubramanian; Govind, Sathe Dhanajay; Venkatraman, Naidu Avinash

PA India

SO U.S. Pat. Appl. Publ., 5 pp., Cont.-in-part of U.S. Ser. No. 365,717.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2004158070 | A1 | 20040812 | US 2003-714724 | 20031117 |
| | US 6649765 | B1 | 20031118 | US 2003-365717 | 20030212 |
| PRAI | US 2003-365717 | A2 | 20030212 | | |

OS CASREACT 141:174080

TI **Hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride)

AB A process for the preparation of 1-benzyl-4-[[(5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (i.e., donepezil HCl; m.p. 210-212°) is described in which 5,6-dimethoxy-2-[(pyridin-4-yl)methyl]inda-1-one is **hydrogenated** with a noble metal catalyst

(e.g., Pd/C) or a non-oxide derivative of a noble metal catalyst in a solvent at 20-100°/10-90 psi-gauge to give 4-[[(5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine which is benzylated with benzyl bromide at 20-80° followed by salification with methanolic HCl.

ST donepezil hydrochloride prepn **hydrogenation** benzylation; benzyldimethoxyindanonylmethylpiperidine hydrochloride prepn **hydrogenation** benzylation

IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(aliphatic, C1-4, solvents; **hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT Ketones, uses
RL: NUU (Other use, unclassified); USES (Uses)
(aromatic, solvents; **hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT **Hydrogenation** catalysts
(chemoselective; Pt-Group metals in a **hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT **Hydrogenation**
(chemoselective; **hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT Benzylation
Quaternization
(**hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT Platinum-group metals
RL: CAT (Catalyst use); USES (Uses)
(**hydrogenation** catalysts in a **hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT Chemoselectivity
(in a **hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT Acids, uses
RL: NUU (Other use, unclassified); USES (Uses)
(organic, solvents; **hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT 7440-44-0, Activated carbon, uses
RL: CAT (Catalyst use); USES (Uses)
(activated, support; **hydrogenation** catalyst in a **hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT 121-44-8, Triethylamine, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(base; in a **hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT 100-39-0, Benzyl bromide 4803-57-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(**hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT **120011-70-3P**, Donepezil hydrochloride
RL: SPN (Synthetic preparation); PREP (Preparation)
(**hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT 7647-10-1, Palladium chloride 10049-07-7, Rhodium chloride 10049-08-8, Ruthenium chloride 10489-46-0, Rhodium sulfate 13566-03-5, Palladium sulfate 41860-99-5, Ruthenium sulfate
RL: CAT (Catalyst use); USES (Uses)
(**hydrogenation** catalyst in a **hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT 7440-05-3, Palladium, uses 7440-16-6, Rhodium, uses 7440-18-8, Ruthenium, uses
RL: CAT (Catalyst use); USES (Uses)
(in a **hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT 1333-74-0, Hydrogen, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(in a **hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT 120014-30-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in a **hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT 64-19-7, Acetic acid, uses 75-09-2, Dichloromethane, uses 141-78-6, Ethyl acetate, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; in a **hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT 7647-01-0, Hydrogen chloride, reactions 7732-18-5, Water, reactions
RL: NUU (Other use, unclassified); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(solvent; in a **hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

IT 471-34-1, Calcium carbonate, uses 1344-28-1, Alumina, uses 7727-43-7, Barium sulfate
RL: CAT (Catalyst use); USES (Uses)
(support; **hydrogenation** catalyst in a **hydrogenation** and benzylation process for the preparation of 1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride))

L6 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:589284 CAPLUS
DN 141:123572
TI Process for preparation of donepezil
IN Reddy, Manne Satyanarayana; Eswaraiah, Sajja; Thippannachar, Mathad Vijayavitthal; Chandrashekar, Elati Ravi Rama; Kumar, Podichetty Anil; Kumar, Kolla Naveen
PA Reddy's Laboratories Limited, India; Reddy's Laboratories, Inc.
SO U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DT Patent
LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2004143121 | A1 | 20040722 | US 2003-626499 | 20030724 |
| PRAI | IN 2002-MA555 | A | 20020724 | | |

OS CASREACT 141:123572

AB An efficient process for preparation of donepezil I is provided. In one embodiment, the process for preparation of donepezil includes suspending a catalyst, which is palladium metal on carbon and the compound II in an alc. solvent and **hydrogenating** the suspension at the hydrogen pressure of from about 1 to about 5 and a temperature of from about 40 to about 90°C till the **hydrogenation** reaction is substantially complete to obtain a compound III which then is converted to donepezil by alkylation with benzyl bromide. The processes of the invention are believed to be simple, eco-friendly, and com. viable.

IT **Hydrogenation**
(process for preparation of donepezil by **hydrogenation** of 5,6-dimethoxy-2-[(pyridin-4-yl)methylene]indan-1-one and subsequent alkylation with benzyl bromide)

IT 7440-05-3, Palladium, uses
RL: CAT (Catalyst use); USES (Uses)
(process for preparation of donepezil by **hydrogenation** of 5,6-dimethoxy-2-[(pyridin-4-yl)methylene]indan-1-one and subsequent alkylation with benzyl bromide)

IT 4803-74-1P 120014-30-4P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of donepezil by **hydrogenation** of 5,6-dimethoxy-2-[(pyridin-4-yl)methylene]indan-1-one and subsequent alkylation with benzyl bromide)

IT **120014-06-4P**, Donepezil
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for preparation of donepezil by **hydrogenation** of 5,6-dimethoxy-2-[(pyridin-4-yl)methylene]indan-1-one and subsequent alkylation with benzyl bromide)

IT 100-39-0, Benzyl bromide 872-85-5, Pyridine-4-carboxaldehyde 2107-69-9, 5,6-Dimethoxyindan-1-one
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparation of donepezil by **hydrogenation** of 5,6-dimethoxy-2-[(pyridin-4-yl)methylene]indan-1-one and subsequent alkylation with benzyl bromide)

IT 64-19-7, Acetic acid, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(process for preparation of donepezil by **hydrogenation** of 5,6-dimethoxy-2-[(pyridin-4-yl)methylene]indan-1-one and subsequent alkylation with benzyl bromide)

IT 67-56-1, Methanol, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; process for preparation of donepezil by **hydrogenation** of 5,6-dimethoxy-2-[(pyridin-4-yl)methylene]indan-1-one and subsequent alkylation with benzyl bromide)

L6 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:527381 CAPLUS
DN 142:74419
TI New approach to N-substituted-1,2,3,6-tetrahydro-pyridine-4-carbaldehyde, a precursor for synthesizing Aricept, isoguvacine, and deethylibophyllidine
AU Tsai, Min-Ruei; Sun, Pei-Pei; Chang, Meng-Yang; Changa, Nein-Chen
CS Department of Chemistry, National Sun Yat-Sen University, Kaohsiung, 804,

Taiwan
SO Journal of the Chinese Chemical Society (Taipei, Taiwan) (2004), 51(3), 613-617
CODEN: JCCTAC; ISSN: 0009-4536
PB Chinese Chemical Society
DT Journal
LA English
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT 503544-95-4P, 1-Benzyl-1,2,3,6-tetrahydro-4-pyridinecarboxaldehyde
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**hydrogenation**, precursor to isoguvacine; new approach to N-substituted piperidine-4-carbaldehydes as precursors for synthesizing Aricept, isoguvacine, and deethylibophyllidine)
IT 64603-90-3P, Isoguvacine 74170-69-7P, Deethylibophyllidine
**120011-70-3P**, Aricept
RL: PNU (Preparation, unclassified); PREP (Preparation)
(new approach to N-substituted piperidine-4-carbaldehydes as precursors for synthesizing Aricept, isoguvacine, and deethylibophyllidine)

L6 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:903267 CAPLUS
DN 139:381380
TI Process for the preparation of 1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-yl)methylpiperidine hydrochloride (donepezil hydrochloride)
IN Vidyadhar, Joshi Shreerang; Venkatraman, Naidu Avinash; Pandurang, Sutar Rajiv
PA USV Limited, BSD Marg., India
SO U.S., 3 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 6649765 | B1 | 20031118 | US 2003-365717 | 20030212 |
| US 2004158070 | A1 | 20040812 | US 2003-714724 | 20031117 |
| PRAI US 2003-365717 | A2 | 20030212 | | |

OS CASREACT 139:381380
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB A process for the preparation of 1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-yl]methylpiperidine hydrochloride (donepezil HCl) is described in which 5,6-dimethoxy-2-(pyridin-4-yl)methyleneinda-1-one is **hydrogenated** with a Platinum-Group metal oxide catalyst in an organic solvent at 20-50°/10-45 psi-gauge, and the resulting 4-[(5,6-dimethoxy-1-indanon)-2-yl]methylpiperidine is benzylated with an benzyl bromide in an organic solvent at 30-80° and salified with methanolic HCl.
IT **Hydrogenation** catalysts
(Pt-Group metal oxides in a process for the preparation of 1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-yl)methylpiperidine hydrochloride (donepezil hydrochloride))
IT **Hydrogenation**
(in a process for the preparation of 1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-yl)methylpiperidine hydrochloride (donepezil hydrochloride))
IT Platinum-group metal compounds
RL: CAT (Catalyst use); USES (Uses)
(oxides; **hydrogenation** catalysts in a process for the preparation of 1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-yl)methylpiperidine hydrochloride (donepezil hydrochloride))

IT Group VIII element oxides
RL: CAT (Catalyst use); USES (Uses)
(platinum-group; **hydrogenation** catalysts in a process for the preparation of 1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-yl)methylpiperidine hydrochloride (donepezil hydrochloride))

IT 1314-15-4, Platinum dioxide
RL: CAT (Catalyst use); USES (Uses)
(**hydrogenation** catalyst in a process for the preparation of 1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-yl)methylpiperidine hydrochloride (donepezil hydrochloride))

IT **120011-70-3P**, Donepezil hydrochloride
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for the preparation of 1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-yl)methylpiperidine hydrochloride (donepezil hydrochloride))

L6 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:464279 CAPLUS
DN 131:102201
TI Process for production of donepezil derivative
IN Iimura, Yoichi
PA Eisai Co., Ltd., Japan
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9936405 | A1 | 19990722 | WO 1999-JP111 | 19990114 |
| | W: CA, US | | | | |
| | RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | CA 2316360 | AA | 19990722 | CA 1999-2316360 | 19990114 |
| | EP 1047674 | A1 | 20001102 | EP 1999-900320 | 19990114 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| | JP 11263774 | A2 | 19990928 | JP 1999-8759 | 19990118 |
| | US 6252081 | B1 | 20010626 | US 2000-582496 | 20000627 |
| PRAI | JP 1998-6908 | A | 19980116 | | |
| | WO 1999-JP111 | W | 19990114 | | |

OS CASREACT 131:102201; MARPAT 131:102201
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The present invention provides a novel industrially or economically preferable process for production of a hydrogen halogenide salt of a donepezil derivative (I; R1 = H, alkoxy; n = 1-4; X = a halogen atom) having an excellent pharmacol. action as medicament, namely, reaction of 1-indanone derivative (II; R = H; R1, n = same as above) with carbonate ester to obtain 2-alkoxycarbonyl-1-indanone derivative (II; R = CO2R2; wherein lower alkyl; R1, n = same as above), followed by reaction with halogenated (4-pyridyl)methyl or a salt thereof and decarboxylation successively to obtain 2-(4-pyridyl)methyl-1-indanone derivative (III; R1, n = same as above), then reaction with halogenated benzyl to obtain quaternary ammonium salt (IV; R1, n = same as above; X = a halogen atom), then reduction to the donepezil derivative (I), and synthetic intermediate thereof. The donepezil derivative is useful as prophylactic or medicament for senile dementia, especially for Alzheimer disease (no data). Thus, 2.00 g 5,6-dimethoxy-2-ethoxycarbonyl-1-indanone was dissolved in DMF and treated with 0.73 g 60% NaH in oil under ice-cooling, and stirred at room temperature for 30 min. The reaction mixture was cooled in an ice-water bath, treated with 1.49 g 4-pyridylmethyl chloride, and stirred under the same condition and then at

room temperature overnight to give 5,6-dimethoxy-2-ethoxycarbonyl-2-(4-pyridylmethyl)-1-indanone as a brown oil, which was refluxed with aqueous ethanol containing KOH for 30 min for decarboxylation to give 5,6-dimethoxy-2-(4-pyridylmethyl)-1-indanone (85% yield through two steps). The latter compound (1.00 g) was dissolved in MeCN under reflux, followed by adding 0.50 mL benzyl bromide, and the refluxing was continued for 2.5 h to quant. give 1-benzyl-4-[(5,6-dimethoxy-1-oxoindan-2-yl)methyl]pyridinium bromide. This compound (1.00 g) was dissolved in MeOH and **hydrogenated** in the presence of 0.1 g platinum oxide fro 3 h at room temperature to give 99% donepezil free base.

ST donepezil prepn senile dementia Alzheimer disease; benzyloxoindanylmethylpyridinium halide **hydrogenation** donepezil

IT **Hydrogenation** catalysts
(platinum oxide; preparation of donepezil derivative from indanone derivative via
catalytic **hydrogenation** of N-benzyl(oxoindanylmethyl)pyridinium halide)

IT **Hydrogenation**
(preparation of donepezil derivative from indanone derivative via catalytic **hydrogenation** of N-benzyl(oxoindanylmethyl)pyridinium halide)

IT 7440-05-3D, Palladium, supported on carbon, uses 11113-84-1, Ruthenium oxide 11129-89-8, Platinum oxide
RL: CAT (Catalyst use); USES (Uses)
(preparation of donepezil derivative from indanone derivative via catalytic **hydrogenation** of N-benzyl(oxoindanylmethyl)pyridinium halide)

IT 4803-57-0P 231283-81-1P 231283-82-2P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of donepezil derivative from indanone derivative via catalytic **hydrogenation** of N-benzyl(oxoindanylmethyl)pyridinium halide)

IT **120011-70-3P**, Donepezil hydrochloride **120014-06-4P**, Donepezil
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of donepezil derivative from indanone derivative via catalytic **hydrogenation** of N-benzyl(oxoindanylmethyl)pyridinium halide)

IT 100-39-0, Benzyl bromide 105-58-8, Diethyl carbonate 616-38-6, Dimethyl carbonate 623-53-0, Methyl ethyl carbonate 623-96-1, Dipropyl carbonate 10445-91-7, 4-Pyridylmethyl chloride 53295-44-6, 5,6-Dimethoxy-2-ethoxycarbonyl-1-indanone 54751-01-8 138761-37-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of donepezil derivative from indanone derivative via catalytic **hydrogenation** of N-benzyl(oxoindanylmethyl)pyridinium halide)

L6 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:425279 CAPLUS
DN 125:86503
TI Process and catalysts for the **hydrogenation** production of 1-benzyl-4-(indan-1-onyl)piperidines from pyridinium salts
IN Lensky, Stephen
PA Bayer A.-G., Germany
SO Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 711756 | A1 | 19960515 | EP 1995-116888 | 19951026 |
| | EP 711756 | B1 | 19980722 | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

| | | | | | |
|---|---|---|---|---|---|
| | DE 4439822 | A1 | 19960829 | DE 1994-4439822 | 19941108 |
| | AT 168676 | E | 19980815 | AT 1995-116888 | 19951026 |
| | ES 2121276 | T3 | 19981116 | ES 1995-116888 | 19951026 |
| | JP 08225527 | A2 | 19960903 | JP 1995-306422 | 19951101 |
| | US 5606064 | A | 19970225 | US 1995-552330 | 19951102 |
| | CA 2162081 | AA | 19960509 | CA 1995-2162081 | 19951103 |
| PRAI | DE 1994-4439822 | A | 19941108 | | |

OS MARPAT 125:86503

TI Process and catalysts for the **hydrogenation** production of 1-benzyl-4-(indan-1-onyl)piperidines from pyridinium salts

AB The title compds. [I; R1-R4 = H, (un)branched alkyl, alkoxy, alkoxycarbonyl, halohen, alkyl- or dialkylamino], useful as CNS agents (no data), are prepared by the **hydrogenation** of pyridinium salts (II; X = halide, tosylate, sulfate). Thus, II (R1-R4 = H, X = Br) was **hydrogenated** with a PtO2 catalyst in MeOH, producing I in 81% yield.

ST benzylpiperidinylindanone prepn CNS agent; pyridinium salt **hydrogenation** prepn benzylpiperidinylindanone

IT **Hydrogenation**
(of pyridinium salts in production of 1-benzyl-4-(indan-1-onyl)piperidines)

IT 7440-06-4, Platinum, uses
RL: CAT (Catalyst use); USES (Uses)
(process and catalysts for the **hydrogenation** production of 1-benzyl-4-(indan-1-onyl)piperidines from pyridinium salts)

IT 83-33-0, Indanone 100-39-0, Benzyl bromide 872-85-5, Pyridine-4-carboxaldehyde 2107-69-9, 5,6-Dimethoxyindan-1-one
RL: RCT (Reactant); RACT (Reactant or reagent)
(process and catalysts for the **hydrogenation** production of 1-benzyl-4-(indan-1-onyl)piperidines from pyridinium salts)

IT 4803-74-1P 4875-89-2P 178551-25-2P 178551-26-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process and catalysts for the **hydrogenation** production of 1-benzyl-4-(indan-1-onyl)piperidines from pyridinium salts)

IT **120014-06-4P** 149874-72-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(process and catalysts for the **hydrogenation** production of 1-benzyl-4-(indan-1-onyl)piperidines from pyridinium salts)

L6 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1993:560046 CAPLUS

DN 119:160046

TI Synthesis and anti-acetylcholinesterase activity of 1-benzyl-4-[(5,6-dimethoxy-1-indanon-2-yl)methyl]piperidine hydrochloride (E2020) and related compounds

AU Sugimoto, Hachiro; Iimura, Youichi; Yamanishi, Yoshiharu; Yamatsu, Kiyomi

CS Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300-26, Japan

SO Bioorganic & Medicinal Chemistry Letters (1992), 2(8), 871-6
CODEN: BMCLE8; ISSN: 0960-894X

DT Journal

LA English

IT 120014-07-5 149874-67-9 149874-68-0 149874-69-1 149874-70-4 149874-71-5 149874-86-2 149874-87-3 149874-88-4 149874-89-5 149874-90-8 149874-91-9 149874-92-0 149874-93-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(**hydrogenation** of)

IT **120011-70-3P** 120012-04-6P 120013-38-9P 120013-45-8P **120014-06-4P** 120014-11-1P 120014-12-2P 120014-30-4P 149874-72-6P 149874-73-7P 149874-74-8P 149874-78-2P 149874-79-3P 149874-80-6P 149874-81-7P 149874-82-8P 149874-83-9P 149874-84-0P 149874-85-1P
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and acetylcholinesterase inhibiting activity of)

L6 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:124398 CAPLUS
DN 118:124398
TI Preparation of (-)-1-benzyl-4-[(5,6-dimethoxy-1-indanon-2-yl)methyl]piperidine by asymmetric **hydrogenation** of (piperidylmethylene)indanone derivative
IN Iimura, Yoichi; Kajima, Takashi; Araki, Shin; Sugimoto, Hachiro; Kiyofuji, Nobuo; Kumobayashi, Hidenori
PA Eisai Co., Ltd., Japan; Takasago Perfumery Co., Ltd.
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | JP 04187674 | A2 | 19920706 | JP 1990-320055 | 19901121 |
| | JP 2965675 | B2 | 19991018 | | |
| PRAI | JP 1990-320055 | | 19901121 | | |

OS CASREACT 118:124398
TI Preparation of (-)-1-benzyl-4-[(5,6-dimethoxy-1-indanon-2-yl)methyl]piperidine by asymmetric **hydrogenation** of (piperidylmethylene)indanone derivative
AB The title compound (I), a known acetylcholine esterase inhibitor useful for the treatment of Alzheimer-type senile dementia, is prepared by asym. **hydrogenation** of (piperidylmethylene)indanone derivative II in the presence of an optically active Ru-phosphine complex, preferably III [A = RuX4, B = NEt3; A = RuHX, B = null; A = null, B = RuAlZ; X = halo; Y = H, NH2, AcNH, SO3H; R1 = H, linear or branched lower alkyl; Al, Z = ClO4, PF6, BF4, R2CO2; R2 = alkyl, haloalkyl, (lower alkyl)phenyl, α-aminoalkyl, α-aminophenylalkyl]. Thus, a solution of 2.0 g II and 42.3 mg RuCl4.[(S)-(-)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl]2.NEt3 complex in 30 mL CH2Cl2 was stirred at H 77 kg/cm2 and 50° for 30 min and then at room temperature for 140 h, evaporated in vacuo, treated with 180 mL 0.1 N HCl (pH 2.0), extracted twice with EtOAc to remove the catalyst, adjusted to pH 9 with aqueous NaHCO3, and extracted with CH2Cl2 to give 85.4% (-)-I of 97.3% ee.
ST benzyldimethoxyindanonylmethylpiperidine prepn acetylcholine esterase inhibitor; piperidine indanoylmethyl acetylcholine esterase inhibitor; Alzheimer senile dementia treatment benzyldimethoxyindanoylmethylpiperidine; ruthenium phosphine asym **hydrogenation** catalyst; piperidylmethyleneindanone asym **hydrogenation**; BINAP ruthenium asym **hydrogenation** catalyst
IT **Hydrogenation**
(stereoselective, of [(benzylpiperidyl)methylene]dimethoxyindanone, (piperidylmethyl)indanone derivative from)
IT **Hydrogenation** catalysts
(stereoselective, ruthenium-phosphine complex, for (benzylpiperidyl)methylene]dimethoxyindanone to (piperidylmethyl)indanone derivative)
IT 1333-74-0, Hydrogen, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(asym. **hydrogenation** by, of (piperidylmethylene)indanone derivative)
IT 145546-80-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(asym. **hydrogenation** of, (piperidylmethyl)indanone derivative from)
IT 103745-89-7 125778-32-7

RL: CAT (Catalyst use); USES (Uses)
(catalyst, for asym. **hydrogenation** of [(benzylpiperidyl)methylene]dimethoxyindanone)

IT 1333-74-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(**hydrogenation**, stereoselective, of [(benzylpiperidyl)methylene]dimethoxyindanone, (piperidylmethyl)indanone derivative from)

IT **120014-06-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as acetylcholine esterase inhibitor)

L6 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1992:591509 CAPLUS
DN 117:191509
TI Preparation of optically active indanone derivative (salts) as acetylcholinesterase inhibitors and dementia-treating agents
IN Iimura, Yoichi; Kajima, Takashi; Araki, Shin; Sugimoto, Hachiro
PA Eisai Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | JP 04021670 | A2 | 19920124 | JP 1990-124515 | 19900515 |
| | JP 3075566 | B2 | 20000814 | | |
| PRAI | JP 1990-124515 | | 19900515 | | |

AB d- And l-1-benzyl-4-(5,6-dimethoxy-1-indanon-2-yl)methylpiperidine (d- and l-I) and their pharmacol. acceptable salts are prepared **Hydrogenation** of 1-benzyl-4-(5,6-dimethoxy-1-indanon-2-ylidenyl)methylpiperidine (preparation given) over Pd/C in THF at room temperature for 6 h and treatment with HCl/AcOEt in CH2Cl2 gave 82% (±)-I.HCl. Salt decomposition and optical resolution of the product gave l-I, which showed IC50 of 4.8 nM against cerebral acetylcholinesterase, vs. 5.9 nM, for (±)-I.

IT **120011-70-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and optical resolution of)

IT **120014-06-4P** 142057-78-1P 142057-80-5P 142097-05-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as acetylcholinesterase inhibitor)

L6 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1991:6302 CAPLUS
DN 114:6302
TI Preparation of piperidine derivatives as cholinergics
IN Sugimoto, Hachiro; Tsuchiya, Yutaka; Higure, Kunizo; Karibe, Norio; Iimura, Yoichi; Sasaki, Atsushi; Yamanishi, Yoshiharu; Ogura, Hiroo; Araki, Shin; Et, Al.
PA Eisai Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 54 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | JP 02169569 | A2 | 19900629 | JP 1988-324620 | 19881222 |
| | JP 2777159 | B2 | 19980716 | | |

PRAI JP 1988-324620 19881222

OS MARPAT 114:6302

AB The title compds. I [J = (substituted) Ph, pyridyl, quinolyl, indenyl, etc.; Z = (R2CH)n, CO(CHR2)n, etc.; n = 0-10; R2 = H, Me; T = N, C; Q = N, C, etc.; K = H, (substituted) Ph, cinnamyl, etc.; q = 1-3; dotted line indicates either single or double bond] were prepared **Hydrogenation** of piperidine derivative II in MeOH containing 5% Rh-C under hydrogen gave a piperidine derivative III. III in vitro exhibited an IC50 of 0.23 μM against acetylcholinesterase.

IT 22065-85-6P **120011-70-3P** 120011-73-6P 120011-79-2P
**120014-06-4P** 120014-18-8P 120014-21-3P 120014-24-6P
130927-86-5P 130927-87-6P 130927-88-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of acetylcholinesterase inhibitor)

IT 120011-67-8P 120011-68-9P 120011-69-0P **120011-70-3P**
120011-72-5P 120011-74-7P 120011-75-8P 120011-76-9P 120011-77-0P
120011-78-1P 120011-85-0P 120011-88-3P 120011-90-7P 120011-91-8P
120011-92-9P 120011-93-0P 120011-94-1P 120011-95-2P 120011-96-3P
120011-97-4P 120011-98-5P 120011-99-6P 120012-00-2P 120012-01-3P
120012-02-4P 120012-03-5P 120012-05-7P 120012-06-8P 120012-08-0P
120012-09-1P 120012-11-5P 120012-12-6P 120012-14-8P 120012-15-9P
120012-16-0P 120012-17-1P 120012-18-2P 120012-20-6P 120012-21-7P
120012-22-8P 120012-23-9P 120012-24-0P 120012-25-1P 120012-26-2P
120012-28-4P 120012-30-8P 120012-31-9P 120012-32-0P 120012-33-1P
120012-34-2P 120012-35-3P 120012-36-4P 120012-38-6P 120012-40-0P
120012-41-1P 120012-42-2P 120012-44-4P 120012-45-5P 120012-46-6P
120012-47-7P 120012-48-8P 120012-49-9P 120012-50-2P 120012-51-3P
120012-52-4P 120012-53-5P 120012-54-6P 120012-55-7P 120012-56-8P
120012-57-9P 120012-58-0P 120012-59-1P 120012-60-4P 120012-61-5P
120012-62-6P 120012-63-7P 120012-64-8P 120012-65-9P 120012-66-0P
120012-67-1P 120012-68-2P 120012-69-3P 120012-70-6P 120012-71-7P
120012-72-8P 120012-73-9P 120012-74-0P 120012-75-1P 120012-76-2P
120012-77-3P 120012-78-4P 120012-79-5P 120012-80-8P 120012-81-9P
120012-82-0P 120012-83-1P 120012-84-2P 120012-85-3P 120012-86-4P
120012-87-5P 120012-88-6P 120012-89-7P 120012-90-0P 120012-91-1P
120012-92-2P 120012-93-3P 120012-94-4P 120012-95-5P 120012-96-6P
120012-98-8P 120012-99-9P 120013-00-5P 120013-01-6P 120013-02-7P
120013-03-8P 120013-04-9P 120013-05-0P 120013-06-1P 120013-07-2P
120013-08-3P 120013-09-4P 120013-10-7P 120013-11-8P 120013-12-9P
120013-13-0P 120013-14-1P 120013-15-2P 120013-16-3P 120013-17-4P
120013-18-5P 120013-19-6P 120013-20-9P 120013-21-0P 120013-22-1P
120013-23-2P 120013-24-3P 120013-25-4P 120013-26-5P 120013-27-6P
120013-28-7P 120013-29-8P 120013-30-1P 120013-31-2P 120013-32-3P
120013-33-4P 120013-34-5P 120013-35-6P 120013-36-7P 120013-37-8P
120013-38-9P 120013-39-0P 120013-41-4P 120013-42-5P 120013-43-6P
120013-44-7P 120013-46-9P 120013-48-1P 120013-49-2P 120013-50-5P
120013-51-6P 120013-52-7P 120013-53-8P 120013-54-9P 120013-55-0P
120013-56-1P 120013-57-2P 120013-58-3P 120013-59-4P 120013-60-7P
120013-61-8P 120013-62-9P 120013-63-0P 120013-65-2P 120013-66-3P
120013-67-4P 120013-68-5P 120013-69-6P 120013-70-9P 120013-71-0P
120013-72-1P 120013-74-3P 120013-75-4P 120013-76-5P 120013-77-6P
120013-78-7P 120013-79-8P 120013-80-1P 120013-81-2P 120013-82-3P
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120013-88-9P 120013-89-0P 120013-90-3P 120013-91-4P 120013-92-5P
120013-93-6P 120013-94-7P 120013-96-9P 120013-97-0P 120013-98-1P
120013-99-2P 120014-00-8P 120014-01-9P 120014-02-0P 120014-03-1P
120014-04-2P 120014-05-3P 120028-72-0P 120028-73-1P 120028-74-2P
120028-75-3P 120028-76-4P 120028-77-5P 120028-79-7P 121202-92-4P
130927-61-6P 130927-62-7P 130927-63-8P 130927-64-9P 130927-65-0P
130927-66-1P 130927-67-2P 130927-68-3P 130927-69-4P 130927-70-7P

130927-71-8P 130927-72-9P 130927-73-0P 130927-74-1P 130927-75-2P
130927-76-3P 130927-78-5P 130927-80-9P 130927-81-0P 130943-87-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as cholinergic)

L6 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1989:173102 CAPLUS
DN 110:173102
TI Preparation of 1-benzyl-4-(substituted alkyl)piperidines and analogs as acetylcholinesterase inhibitors
IN Sugimoto, Hachiro; Tsuchiya, Yutaka; Higurashi, Kunizou; Karibe, Norio; Iimura, Yuoichi; Sasaki, Atsushi; Yamanashi, Yoshiharu; Ogura, Hiroo; Araki, Shin; et al.
PA Eisai Co., Ltd., Japan
SO Eur. Pat. Appl., 103 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 296560 | A2 | 19881228 | EP 1988-109924 | 19880622 |
| | EP 296560 | A3 | 19900502 | | |
| | EP 296560 | B1 | 19960228 | | |
| | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | FI 8802716 | A | 19881223 | FI 1988-2716 | 19880608 |
| | FI 95572 | B | 19951115 | | |
| | FI 95572 | C | 19960226 | | |
| | NO 8802696 | A | 19881223 | NO 1988-2696 | 19880617 |
| | NO 177590 | B | 19950710 | | |
| | NO 177590 | C | 19951018 | | |
| | ZA 8804338 | A | 19890329 | ZA 1988-4338 | 19880617 |
| | US 4895841 | A | 19900123 | US 1988-209339 | 19880620 |
| | DK 8803379 | A | 19881223 | DK 1988-3379 | 19880621 |
| | DK 172337 | B1 | 19980330 | | |
| | HU 50768 | A2 | 19900328 | HU 1988-3160 | 19880621 |
| | HU 214592 | B | 19980428 | | |
| | DD 283377 | A5 | 19901010 | DD 1988-316988 | 19880621 |
| | RU 2009128 | C1 | 19940315 | RU 1988-4356030 | 19880621 |
| | CA 1338808 | A1 | 19961224 | CA 1988-569944 | 19880621 |
| | AU 8818216 | A1 | 19881222 | AU 1988-18216 | 19880622 |
| | AU 627151 | B2 | 19920820 | | |
| | CN 1030752 | A | 19890201 | CN 1988-103779 | 19880622 |
| | CN 1024547 | B | 19940518 | | |
| | JP 01079151 | A2 | 19890324 | JP 1988-153852 | 19880622 |
| | JP 2578475 | B2 | 19970205 | | |
| | EP 579263 | A1 | 19940119 | EP 1993-113146 | 19880622 |
| | EP 579263 | B1 | 19980916 | | |
| | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | EP 673927 | A1 | 19950927 | EP 1995-104080 | 19880622 |
| | EP 673927 | B1 | 20010919 | | |
| | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | AT 134618 | E | 19960315 | AT 1988-109924 | 19880622 |
| | ES 2083359 | T3 | 19960416 | ES 1988-109924 | 19880622 |
| | EP 742207 | A1 | 19961113 | EP 1996-110252 | 19880622 |
| | EP 742207 | B1 | 20010829 | | |
| | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | AT 171161 | E | 19981015 | AT 1993-113146 | 19880622 |
| | ES 2121039 | T3 | 19981116 | ES 1993-113146 | 19880622 |
| | EP 1116716 | A1 | 20010718 | EP 2001-102878 | 19880622 |
| | R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | AT 204862 | E | 20010915 | AT 1996-110252 | 19880622 |

| | | | | | |
|---|---|---|---|---|---|
| | AT 205828 | E | 20011015 | AT 1995-104080 | 19880622 |
| | ES 2160747 | T3 | 20011116 | ES 1996-110252 | 19880622 |
| | ES 2164720 | T3 | 20020301 | ES 1995-104080 | 19880622 |
| | US 5100901 | A | 19920331 | US 1989-423349 | 19891018 |
| | CN 1073939 | A | 19930707 | CN 1992-112982 | 19921110 |
| | CN 1034015 | B | 19970212 | | |
| | CN 1071417 | A | 19930428 | CN 1992-112995 | 19921112 |
| | CN 1038839 | B | 19980624 | | |
| | JP 07252216 | A2 | 19951003 | JP 1994-291169 | 19941125 |
| | JP 2733203 | B2 | 19980330 | | |
| | CA 1340192 | A1 | 19981215 | CA 1995-616996 | 19950424 |
| | FI 9502850 | A | 19950609 | FI 1995-2850 | 19950609 |
| | FI 9602753 | A | 19960704 | FI 1996-2753 | 19960704 |
| | FI 103969 | B1 | 19991029 | | |
| | DK 9601082 | A | 19961003 | DK 1996-1082 | 19961003 |
| | DK 175246 | B1 | 20040719 | | |
| | DK 9601083 | A | 19961003 | DK 1996-1083 | 19961003 |
| | JP 10067739 | A2 | 19980310 | JP 1997-186306 | 19970711 |
| | JP 3078244 | B2 | 20000821 | | |
| | GR 3036553 | T3 | 20011231 | GR 2001-401406 | 20010906 |
| PRAI | JP 1987-155058 | A | 19870622 | | |
| | FI 1988-2716 | A | 19880608 | | |
| | US 1988-209339 | A3 | 19880620 | | |
| | CA 1988-569944 | A3 | 19880621 | | |
| | CN 1988-103779 | A | 19880622 | | |
| | EP 1988-109924 | A3 | 19880622 | | |
| | EP 1995-104080 | A3 | 19880622 | | |
| | JP 1994-291169 | A3 | 19880622 | | |

OS MARPAT 110:173102

AB The title compds. [I; B = (CHR2)r, CO(CHR2)r, NR4(CHR2)r, etc.; J = alkyl, cyclic amide residue, R1CH:CH, (un)substituted Ph, cyclohexyl, heterocyclyl, mono- or divalent (un)substituted indanyl, PhCOCHMe, etc.; K = H, acyl, (un)substituted Ph, aralkyl, etc.; Q = N, C (sic), NO; R1 = H, alkoxycarbonyl; R2 = H, Me; R4 = H, alkyl, acyl, (un)substituted Ph; PhCH2, etc.; T = N, C; q = 1-3; r = 0-10; JB and BT may be doubly bonded] were prepared Ph3PCH2OMeCl was stirred 30 min at 0° with BuLi in Et2O after which 1-benzyl-4-piperidone was added and the mixture stirred at room temperature 3 h to give an oil which was refluxed 3 h in aqueous MeOH containing HCl to give 1-benzylpiperidine-4-carboxaldehyde (II). 5,6-Dimethoxy-1-indanone was stirred with (Me2CH)2NLi in THF containing HMPA after which II was added and the mixture stirred 2 h to give indanonylidenemethylpiperidine III (R5R6 = bond) which was **hydrogenated** over Pd/C to give, after acidification, III.HCl (R5 = R6 = H). The latter gave 55% inhibition of scopolamine-induced learning impairment in rats at 0.125 mg/kg orally.

IT

| | | | | |
|---|---|---|---|---|
| 120011-67-8P | 120011-68-9P | 120011-69-0P | **120011-70-3P** | |
| 120011-71-4P | 120011-72-5P | 120011-73-6P | 120011-74-7P | 120011-75-8P |
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| 120013-87-8P | 120013-88-9P | 120013-89-0P | 120013-90-3P | 120013-91-4P |
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| 120014-02-0P | 120014-03-1P | 120014-04-2P | 120014-05-3P | |

**120014-06-4P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as acetylcholinesterase inhibitor)

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     (FILE 'HOME' ENTERED AT 07:11:20 ON 15 FEB 2005)

     FILE 'REGISTRY' ENTERED AT 07:11:29 ON 15 FEB 2005
L1            1 S DONEPEZIL/CN

     FILE 'CAPLUS' ENTERED AT 07:11:53 ON 15 FEB 2005
L2           18 S L1/P

     FILE 'REGISTRY' ENTERED AT 07:13:43 ON 15 FEB 2005
L3            1 S DONEPEZIL HYDROCHLORIDE/CN

     FILE 'CAPLUS' ENTERED AT 07:14:11 ON 15 FEB 2005
L4           26 S L3/P
L5            4 S (L2 OR L4) AND ?CYCLIZ?
L6           13 S (L2 OR L4) AND HYDROGENA?

=> s l6 and (palladium or pt)
        146102 PALLADIUM
        227263 PT
L7            6 L6 AND (PALLADIUM OR PT)

=> s l7 and alcohol?
        376798 ALCOHOL?
L8            2 L7 AND ALCOHOL?

=> d bib 1-2

L8   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2004:802718  CAPLUS
DN   141:314158
TI   Process for the preparation of donepezil and derivatives thereof
IN   Kumar, Yatendra; Prasad, Mohan; Nath, Asok; Maheshwari, Nitin
PA   Ranbaxy Laboratories Limited, India
SO   PCT Int. Appl., 25 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
     --------------      ----   --------    -------------------      --------
PI   WO 2004082685        A1    20040930    WO 2004-IB843            20040322
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
             SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
PRAI IN 2003-DE352        A     20030321
OS   CASREACT 141:314158; MARPAT 141:314158
RE.CNT  6     THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8   ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2004:652671  CAPLUS
DN   141:174080
TI   Hydrogenation and benzylation process for the preparation of
```

1-benzyl-4-[[5,6-dimethoxy-1-indanon)-2-yl]methyl]piperidine hydrochloride (donepezil hydrochloride)

IN Radhakrishnan, Tarur Venkatasubramanian; Govind, Sathe Dhanajay; Venkatraman, Naidu Avinash

PA India

SO U.S. Pat. Appl. Publ., 5 pp., Cont.-in-part of U.S. Ser. No. 365,717.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 2004158070 | A1 | 20040812 | US 2003-714724 | 20031117 |
| US 6649765 | B1 | 20031118 | US 2003-365717 | 20030212 |
| PRAI US 2003-365717 | A2 | 20030212 | | |

OS CASREACT 141:174080

=> s l7 not l8
L9 4 L7 NOT L8

=> d bib 1-4

L9 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:29309 CAPLUS

DN 142:113913

TI Catalytic **hydrogenation** process for the preparation of intermediates for acetyl cholinesterase inhibitors

IN Reddy, Bandi Parthasaradhi; Reddy, Kura Rathnakar; Reddy, Rapolu Raji; Reddy, Dasari Muralidhara

PA Hetero Drugs Limited, India

SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2005003092 | A1 | 20050113 | WO 2003-IN232 | 20030701 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI WO 2003-IN232 20030701

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:589284 CAPLUS

DN 141:123572

TI Process for preparation of donepezil

IN Reddy, Manne Satyanarayana; Eswaraiah, Sajja; Thippannachar, Mathad Vijayavitthal; Chandrashekar, Elati Ravi Rama; Kumar, Podichetty Anil; Kumar, Kolla Naveen

PA Reddy's Laboratories Limited, India; Reddy's Laboratories, Inc.

SO U.S. Pat. Appl. Publ., 7 pp.

CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 2004143121 | A1 | 20040722 | US 2003-626499 | 20030724 |
| PRAI IN 2002-MA555 | A | 20020724 | | |

OS CASREACT 141:123572

L9 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:903267 CAPLUS
DN 139:381380
TI Process for the preparation of 1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-yl)methylpiperidine hydrochloride (donepezil hydrochloride)
IN Vidyadhar, Joshi Shreerang; Venkatraman, Naidu Avinash; Pandurang, Sutar Rajiv
PA USV Limited, BSD Marg., India
SO U.S., 3 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 6649765 | B1 | 20031118 | US 2003-365717 | 20030212 |
| US 2004158070 | A1 | 20040812 | US 2003-714724 | 20031117 |
| PRAI US 2003-365717 | A2 | 20030212 | | |

OS CASREACT 139:381380
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:464279 CAPLUS
DN 131:102201
TI Process for production of donepezil derivative
IN Iimura, Yoichi
PA Eisai Co., Ltd., Japan
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9936405 | A1 | 19990722 | WO 1999-JP111 | 19990114 |
| W: CA, US | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2316360 | AA | 19990722 | CA 1999-2316360 | 19990114 |
| EP 1047674 | A1 | 20001102 | EP 1999-900320 | 19990114 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 11263774 | A2 | 19990928 | JP 1999-8759 | 19990118 |
| US 6252081 | B1 | 20010626 | US 2000-582496 | 20000627 |
| PRAI JP 1998-6908 | A | 19980116 | | |
| WO 1999-JP111 | W | 19990114 | | |

OS CASREACT 131:102201; MARPAT 131:102201
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT